Washington State Health Care Authority

Bisphosphonates

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- Guideline Recommendations / Evidence Review
- Utilization and Spend
- Recommendation

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Background

- Bisphosphonates were first approved in the 1990s and are the most widely used drugs to treat osteoporosis[1].
- Bisphosphonates can prevent or treat osteoporosis by inhibiting the bone resorption activity of osteoclasts. This leads to an increase in bone mineral density (BMD), which in turn leads to a reduced risk of fracture.
- Current FDA-approved bisphosphonates include:
  - alendronate (oral tablets, 5 mg daily or 35 mg weekly for prevention; 10 mg daily or 70 mg weekly for treatment)
  - ibandronate (oral tablets, 150 mg monthly; intravenous injection, 3mg every 3 months)
  - risendronate (oral tablets, 5 mg daily or 35 mg weekly or 75 mg for two consecutive days once per month or 150 mg monthly)
  - zoledronic acid (intravenous solution, 5 mg once every 2 years for prevention; 5 mg once every year for treatment)

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FDA Approved Uses

Agent	Treatment of osteoporosis in postmenopausal women	Prevention of osteoporosis in postmenopausal women	Treatment to increase bone mass in men with osteoporosis	Treatment of glucocorticoid-induced osteoporosis	Treatment of Paget's disease of bone
alendronate	Y	Y	Y	Y	Y
ibandronate	Y	Y	N	N	N
risedronate	Y	Y	Y	Y	Y
zoledronic acid	Y	Y	Y	Y	Y

Guideline Recommendations

- American College of Physicians (2017) recommends:
  - alendronate, risedronate, zoledronic acid, or denosumab to reduce hip and vertebral fractures in women with known osteoporosis[2]
  - bisphosphonates to reduce vertebral fracture in men who have clinically recognized osteoporosis[2]

- American Association of Clinical Endocrinologists (2016) recommends:
  - alendronate, risedronate, zoledronic acid, or denosumab for patients with no prior fragility fractures or moderate fracture risk[1]
  - No head-to-head trials with clinical outcomes (i.e. fractures) but current evidence suggests 4 above therapies offer “broad spectrum” anti-fracture efficacy[1]

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Summary of Evidence from American College of Physicians[2]

Agent	Effect on fracture risk (level of evidence)			Adverse effects
	Vertebral	Non-vertebral	Hip	
Alendronate	Improves (high quality)	Improves (high quality)	Improves (high quality)	Mild upper GI symptoms (high quality)
Ibandronate	Improves (high quality)	Uncertain	Uncertain	Mild upper GI symptoms (high quality); myalgias, cramps and limb pain
Risedronate	Improves (high quality)	Improves (high quality)	Improves (high quality)	Mild upper GI symptoms (high quality)
Zoledronic acid	Improves (high quality) in osteoporotic men (moderate quality)	Improves (high quality)	Improves (high quality)	Mild upper GI symptoms, hypocalcaemia, influenza-like symptoms (high quality); atrial fibrillation; arthritis and arthalgias, headaches, uveitis

2. Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update From the American College of Physicians. Ann Intern Med. 2017 Jun 6;166(11):818-839.

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Evidence Review

- An AHRQ-funded systematic review (n=315) from 2014 found:
  - the NNT for bisphosphonates is 60-89 to prevent 1 vertebral fracture over 1-3 years of treatment [60 to 267 person-years][3]
  - the NNT for bisphosphonates is 50-60 to prevent 1 non-vertebral fracture over 1-3 years of treatment [50 to 180 person-years][3]
  - an estimate of 72 to 956 events of mild upper gastrointestinal symptoms will occur per 1000 persons treated with bisphosphonates[3]
- Cochrane reviews of bisphosphonate found:
  - alendronate offers a clinically important benefit in the secondary prevention of vertebral, non-vertebral, hip, and wrist fractures[4]. For primarily prevention, only vertebral fractures were rated as having a clinically important reduction[4].
  - risendronate offers a clinically important benefit in the secondary prevention of vertebral, non-vertebral, and hip fractures but not wrist[5]. There were no statistically significant reductions in the primary prevention of vertebral and non-vertebral fractures[5].

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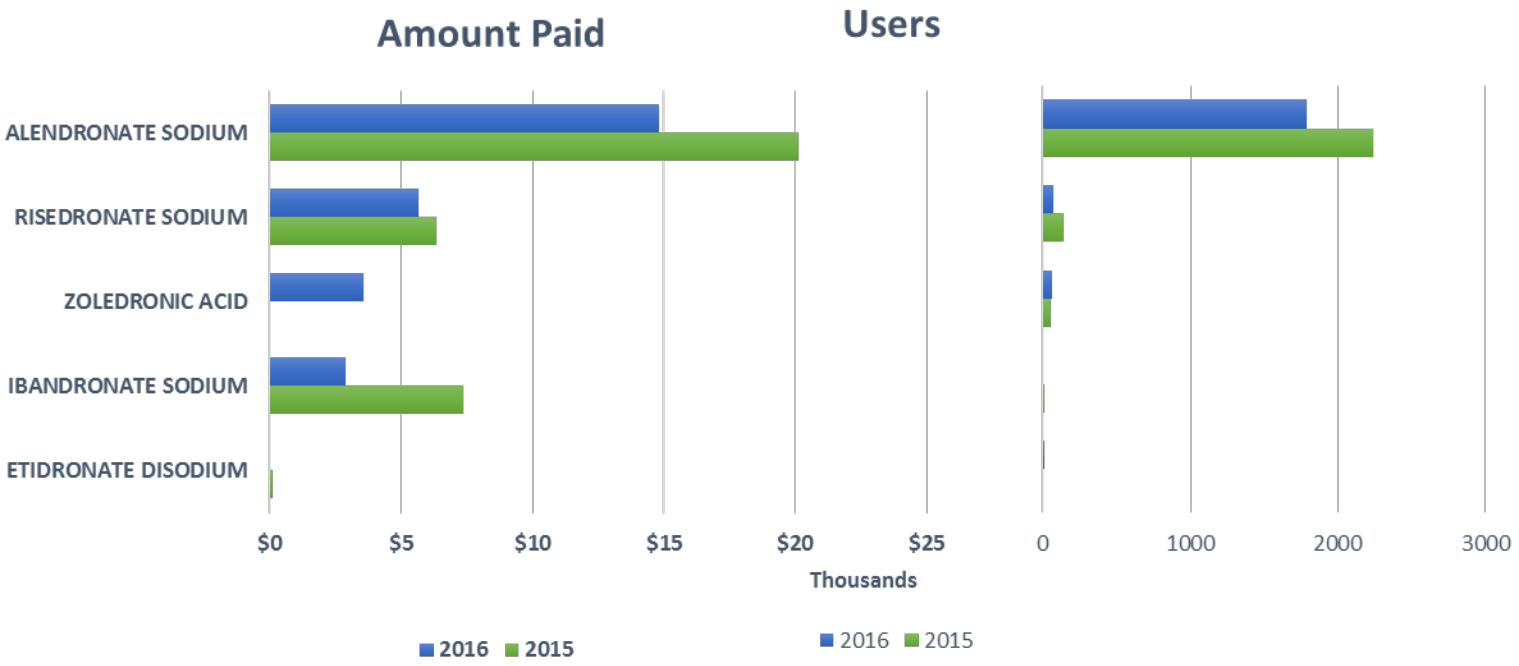
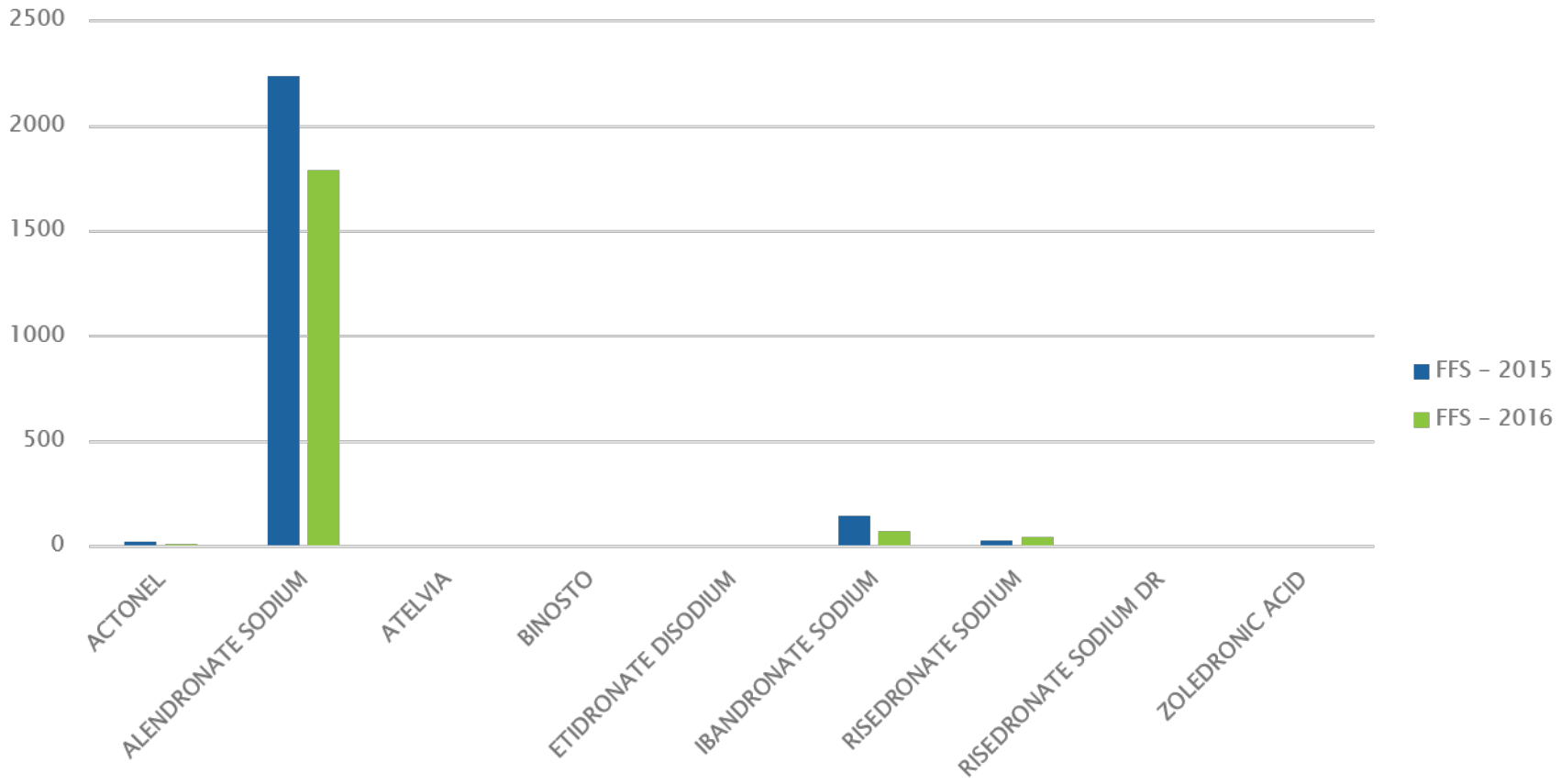
Bisphosphonate Utilization



Bisphosphonate Utilization



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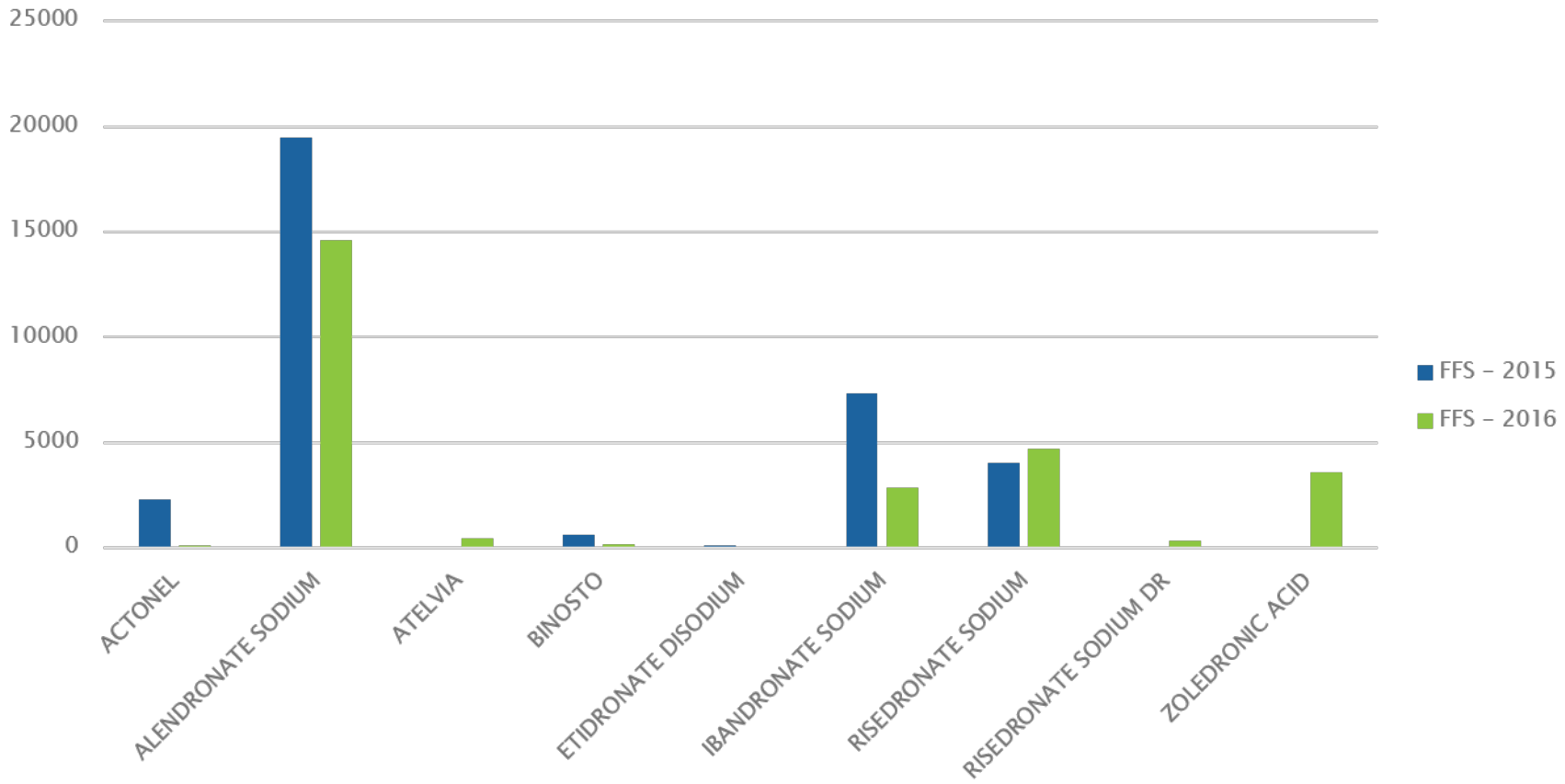

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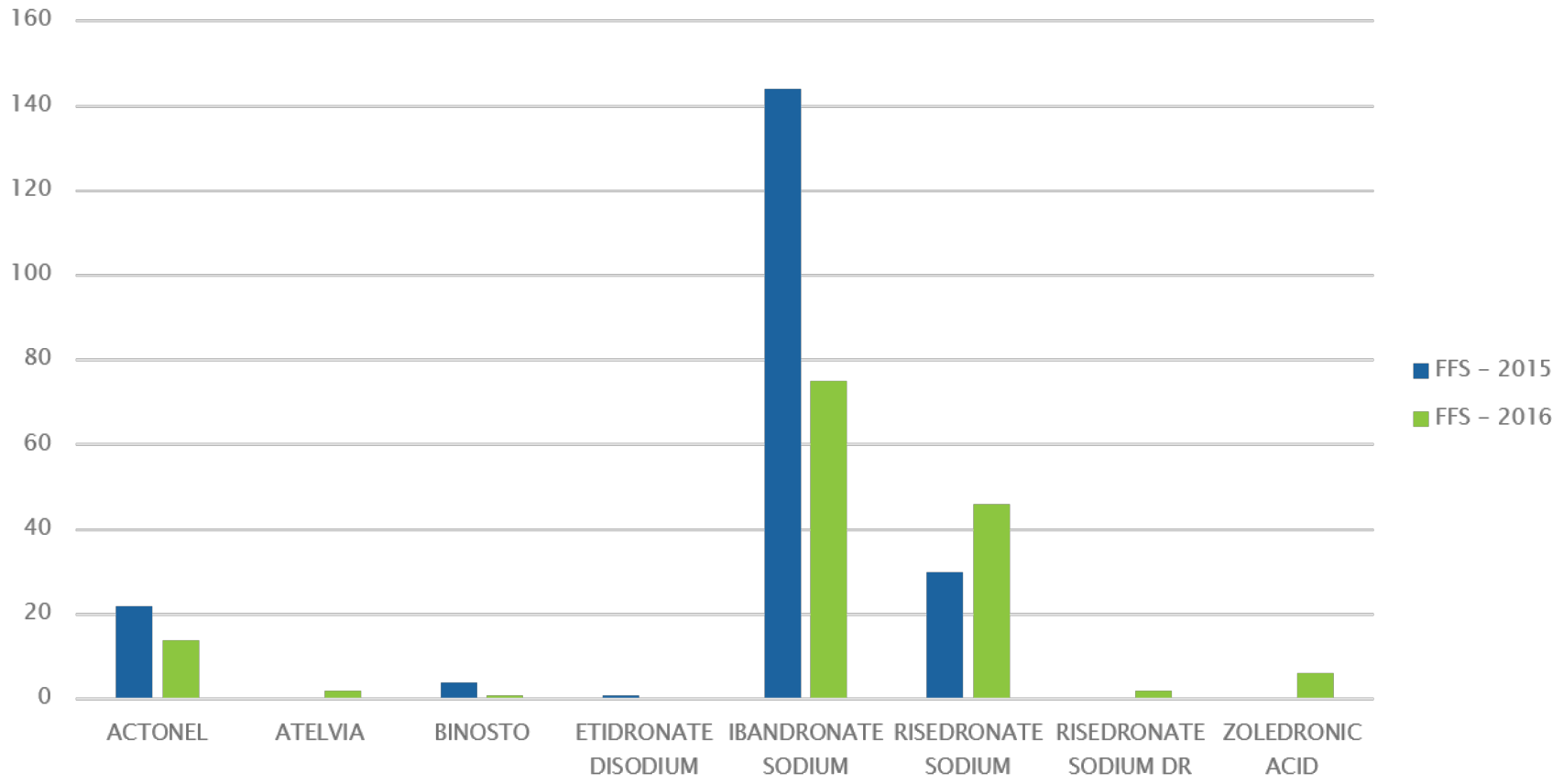

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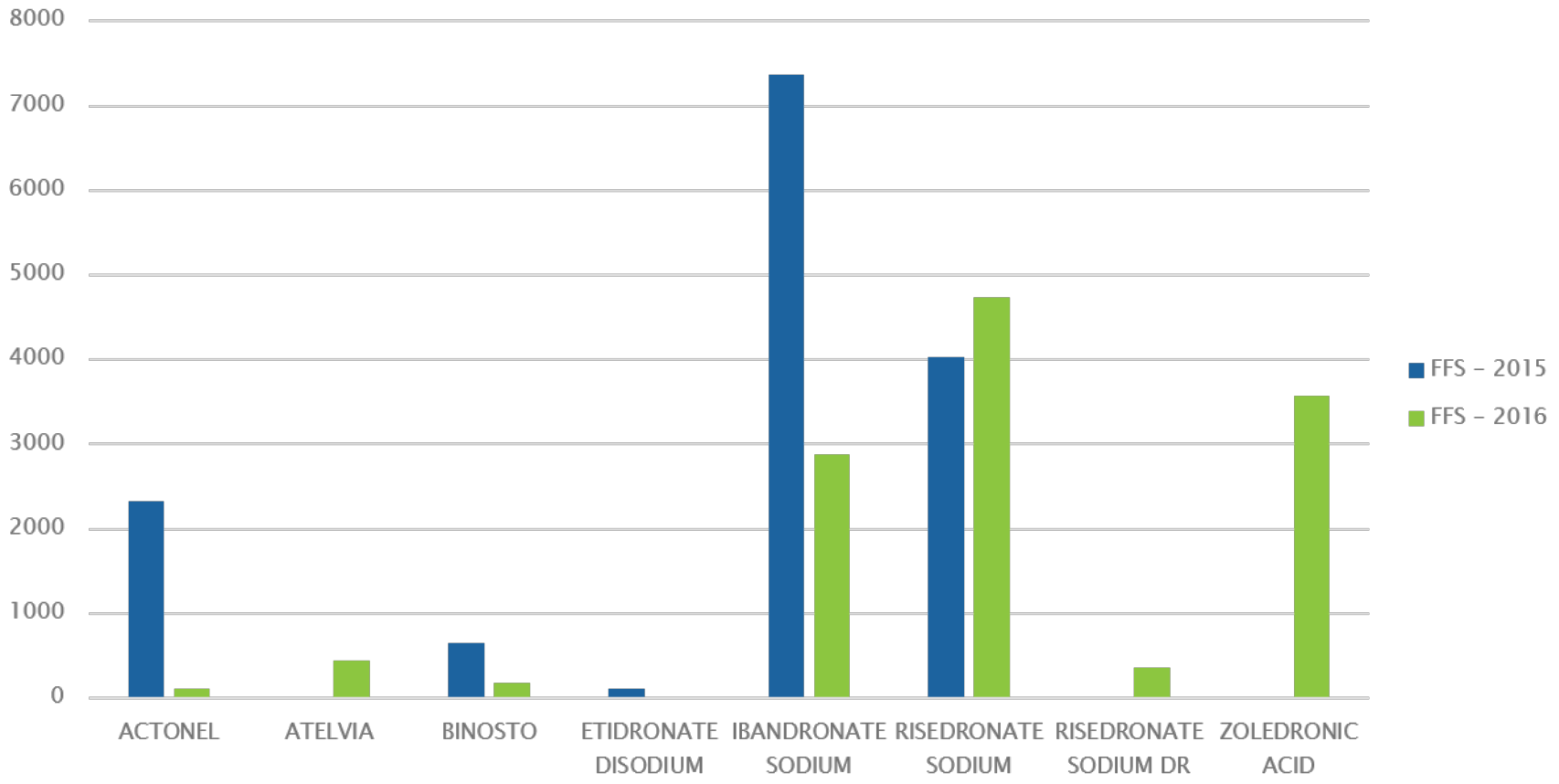

Recommendations

- Based on the review of practice guidelines, clinical evidence, and current costs and utilization, we recommend:
  - alendronate be the preferred bisphosphonate for Medicaid FFS
  - risedronate be the second option after trial and failure of alendronate
  - all other bisphosphonates be the third option after trial and failure of alendronate and risedronate
  - zoledronic acid be available for patients demonstrating a contraindicated to oral bisphosphonate therapy

Motion

- **Motion:** "I move the Medicaid Fee-for-Service Program implement the limitations for the bisphosphonates listed on slide 13 as recommended."

- Motion: Storhaug
- 2nd: Schwilke
- Vote: Passed

Citations

1. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis – 2016. Endocr Pract. 2016 Sep 2;22(Suppl 4):1-42.
2. Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update From the American College of Physicians. Ann Intern Med. 2017 Jun 6;166(11):818-839.
3. Crandall CJ, Newberry SJ, Diamant A, et al. Comparative effectiveness of pharmacologic treatments to prevent fractures: an updated systematic review. Ann Intern Med. 2014 Nov 18;161(10):711-23.
4. Wells GA, Cranney A, Peterson J, et al. Alendronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD001155.
5. Wells GA, Cranney A, Peterson J, et al. Risedronate for the primary and secondary prevention of osteoporotic fractures in postmenopausal women. Cochrane Database of Systematic Reviews 2008, Issue 1. Art. No.: CD004523.

Questions?

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